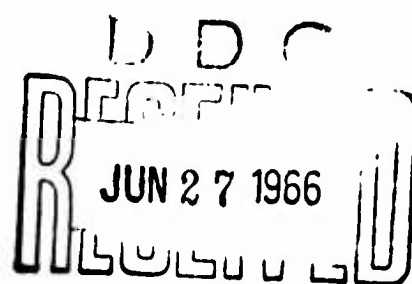


AFOSR 66-0956

FINAL REPORT

GRANT AF-AFOSR 9-64

October 1, 1963 - March 31, 1965



Investigations in the Field of Relational Biology

I. Introduction.

During the period of the above-cited grant, we have continued our studies of the relational properties of organisms, mainly in terms of the class of relational metabolic models which we have termed (M, R)-systems. Our work with respect to these systems may roughly be divided into three parts: (a) The properties of individual (M, R)-systems and biologically interesting classes of such systems; (b) The realizability of individual systems and classes of systems, in terms of specific physico-chemical systems; and (c) The formalization of a notion of optimal realization.

Let us briefly review the definition of the (M, R)-systems and some of their salient features, as described in detail in previous reports and proposals. It is well known that any arbitrary input-output system may be regarded as an array of components which satisfy a number of input-output relations characteristic of the system. Moreover, the components of the system may each be represented by a mapping defined on an appropriate set (input-set), with values in an output-set. Thus a system is just an array of mappings with certain relations imposed on the domains and ranges of these mappings.

Given an arbitrary system M, let us associate with each component (mapping) f of M a new component, which produces as outputs copies of mappings like f , and which accepts as inputs certain outputs of the system M. The new system, consisting of the original system M and the new components we have adjoined, is what basically we called an (M, R)-system. It may serve to fix ideas to call the components of the system M the "metabolic" components of the (M, R)-system, and the adjoined components the "genetic" components of the system.

These (M, R)-systems are sufficiently structured to enable us to prove a number of biologically meaningful results. For one thing, we can show that under certain natural conditions there will exist induced maps intrinsic to the system which will replicate the "genetic" components of the system. We can introduce a notion of re-establishability in these systems, which specifies the conditions under which an (M, R)-system will replace a particular metabolic component which has been inhibited, and we can show that every (M, R)-system has a non-re-establishable component. The biological significance of these and related results is clear.

We have also been able to show that, under certain conditions, an alteration of the inputs to the system can result in an alteration of the "metabolic" structure of the system. This observation leads to what we call the central problem of the theory; namely, when can such an alteration of "metabolic" structure be reversed by a further sequence of environmental

alterations, or more generally, when is it possible to force a given system to assume a pre-assigned "metabolic" structure by an appropriate sequence of environmental alterations? The biological importance of this problem arises from the fact that problems of differentiation and neoplasia are of this form.

The solution to this central problem rests partly on the particular structure of individual (M, R) -systems, and partly on the universe of discourse (or category) from which our systems are built. The major task is to identify how the structure of the category in which we are operating manifests itself in terms of the individual (M, R) -systems built from this category.

The central problem of (M, R) -systems is closely related to problems in other disciplines, for instance to the controllability of dynamical systems, or the strong connectedness of sequential machines. Indeed, the (M, R) -systems stand formally somewhere between the dynamical systems (which are continuous-time automata) and the sequential machines (discrete-time automata), and the problems which arise in the theory of (M, R) -systems have thrown light on these other areas. Indeed, part of our research has been devoted to constructing a unified formalism which is capable of answering homologous questions in each of these areas.

Let us now describe the work accomplished during the period of the above-mentioned grant.

II. Properties of (M, R) -Systems.

During the grant period we undertook the construction of a formalism common to discrete and continuous-time automata and the (M, R) -systems. Our first results were concerned with the relation between (M, R) -systems over a given category and discrete-time automata (sequential machines). In the two papers written during the grant period which deal with this aspect (Rosen, 1964a, 1964b), we showed how the (M, R) -systems could be represented by a particular class of sequential machine, and related the central problem to the strong connectedness of such machines. We showed that unless rather strong restrictions were placed on the underlying category, most (M, R) -systems (in a sense made precise in these papers) must fail to correspond to strongly connected machines, and thus the central problem has in general a negative solution for these systems. These restrictions take the form of an upper bound to the richness of the underlying category. Such results are interesting because in previous work (Rosen, Bulletin of Mathematical Biophysics, 25 (1963), 41-50, 231-241) we previously found that a lower bound on the richness of the underlying category was necessary in order to yield an interesting class of (M, R) -systems over the category. Considerations of this kind are closely related to problems of realizability, which we discuss below.

A third paper (Rosen, 1965) generalizes the concept of re-establishability to systems in which finite lags are defined, and shows that there is essentially no difference (at least as far as re-establishability is concerned) between the case where lags are present and where they are not.

III. Realizability of (M, R)-Systems.

In earlier work (Rosen, Bulletin of Mathematical Biophysics, 24 (1962), 375-393), we showed that the physical realizability of abstract systems is closely connected with the completeness of the physical laws governing real systems. In particular, we showed that Church's Thesis, which in principle relates the class of "constructable" automata to a precise algorithmic procedure, is a valid tool only if, roughly speaking, we can extract the program of a machine from the equations of motion of the machine considered as a real physical system. It is not clear that this restriction is satisfied by physical laws. In the grant period, we gave a number of arguments (Rosen, 1964c) which may indicate that this restriction is indeed not satisfied in physics, and hence that the realizability problem may not be solvable within the context of physics as presently understood.

However, we can assume that if an abstract functional organization can be realized at all, it is possible to define a class of real physical systems which realize that organization, even if we cannot effectively specify the full class of such realizations. The question then arises how we may identify and study individual members of such a class. One solution to this problem (which must be solved in order to relate the results of relational considerations to the physico-chemical knowledge we possess concerning real biological systems) lies in the notion of an optimal realization.

IV. Optimality in Relational Biology.

It is obvious that considerations of optimal design, working through selection pressure, have played a decisive role in the structure of real organisms. Hugo Martinez (1964) attempted to formulate a notion of selective advantage which would apply (M, R)-systems, and which would restrict the class of (M, R)-systems which we might find realized by actual biological organisms. His idea was to consider as an index of such an advantage the difference between the number of re-establishable components of the system and the number of central components (where a central component is one whose inhibition results in the inhibition of the entire system; under appropriate conditions the existence of central components can be inferred from the previously-mentioned theorem on non-re-establishability). Like any optimality principle, Martinez' suggestion serves to cut down the size of the set of systems which we need to consider in relating our theory to the "real biological world."

Any optimality problem takes the form of choosing a suitable "cost function" over a set of a priori solutions to a particular problem, and finding that solution which minimizes the cost. These problems are widespread through biology and have important theoretical implications. As far as relational biology, and in particular, the study of realizability, is concerned it immediately suggests itself that we can pick individual physical realizations of an abstract organization from a class of such realizations by (a) fixing by fiat a physical component of the system, and then (b) optimizing the rest of the system around that choice of physical component with

respect to a suitable cost functional. Thus for instance, if we wish to study individual realizations of amplifying devices, we might specify that the amplifier contain a particular kind of triode, and that the cost of construction of the amplifier be minimal. These constraints are enough to specify the physical properties of the entire amplifier rather completely. In a short expository paper (Rosen, 1965) we developed this idea and indicated some of its applications.

Our study of optimality led to the preparation of the manuscript for a monograph entitled Optimality Principles in Biology, in which we indicated how a large number of apparently diverse areas in biology were unified by the explicit application of optimality techniques. This monograph is mainly expository, but contains a number of new results (mainly an elaborate development of the ideas first presented in Rosen, Bulletin of Mathematical Biophysics, 24 (1962), 279-290).

We expect that ideas of this kind will have, among other things, application to the physical specification of long extinct transitional biological forms, especially those postulated in discussions of the origin of life, and to the possibility of realizing biological organizations (such as the (M, R)-systems) in terms of non-biological physical structures (cf. Rosen, "Relational Biology and Bionics," IEEE Trans. on Military Electronics, Vol. MIL-7 (1963), 160-162); this may have a bearing both on engineering and on the study of extra-terrestrial life.

V. Bibliography of Papers Resulting from Grant.

1. Martinez, H. 1964. "Toward an Optimal Design Principle in Relational Biology." Bull. Math. Biophysics, 26, 351-365.
2. Rosen, R. 1964a. "Abstract Biological Systems as Sequential Machines." Bull. Math. Biophysics, 26, 103-111.
3. _____. 1964b. "Abstract Biological Systems as Sequential Machines II: Strong Connectedness." Bull. Math. Biophysics, 26, 239-246.
4. _____. 1964c. "The Gibbs Paradox and the Distinguishability of Physical Systems." Philosophy of Science, 31, 232-236.
5. _____. 1965a. "Some Comments on Re-establishability." Bull. Math. Biophysics, 27 (Special Issue), 11-14.
6. _____. 1965b. "Biological and Physical Realizations of Abstract Metabolic Models." Proc. Second International Symposium on Quantitative Biology of Metabolism. In press.
7. _____. Optimality Principles in Biology. London: Butterworth and Company. In press.

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The studies reported herein are concerned with the structure and properties of a class of relational models of simple organisms. Some important problems relating to the behavior of these systems in altering environments are related to the properties of associated sequential machines and thence to control problems in dynamical systems. Questions of realizability of these abstract systems are considered in some detail, and the formulation of a general optimality principle, which would allow us to relate the abstract model to specific physico-chemical realizations (i.e., real organisms) is discussed. Some implications of this study, both for important problems in biology, and for the study of nonbiological (i.e., engineering or extraterrestrial) realizations of biological organizations are described.

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